PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
PATENT EXAMINING OPERATION

First Named Inventor: Charli KRUSE

Serial No: 10/820,430 Group Art Unit: 1632

Filed: April 8, 2004 Examiner: Joanne Hama

Att. Docket No.: B1180/20026 Confirmation No.: 7174

For: ISOLATED ADULT PLURIPOTENT STEM CELLS AND METHODS FOR ISOLATING AND CULTIVATING THEREOF

DECLARATION OF CHARLI KRUSE UNDER 37 CFR § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Charli Kruse, Ph.D., a citizen of Germany, hereby declares and states:

1. The resume attached as Exhibit A accurately reflects my professional credentials.
2. I am the sole inventor named in the above-identified application.
3. My research is funded in part by Fraunhofer-Gesellschaft zur Förderung der angewandten Forschung e.V., the assignee of the above-identified application.
4. I understand from my review of the application that claims 1-14 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement for isolated pluripotent adult stem (IPAS) cells from any species of vertebrate obtained from any exocrine gland tissue, wherein said IPAS cells differentiate into various cell types.

5. I understand from attorneys for the assignee that the standard for determining compliance with the enablement requirement of Section 112, first paragraph, is whether the original specification contained sufficient information regarding the subject matter of the claims as to enable one reasonably skilled in the pertinent art to make and use the claimed invention without undue experimentation. While I am not an expert in patent law, my experience and educational background, particularly as a researcher and private lecturer at the University of Lübeck, enable me to render an informed opinion as to the facts underlying the determination of enablement, including the level of ordinary skill in the art, information known in the art at the time of the invention, and what constitutes undue experimentation to one of ordinary skill in the art. For the reasons discussed below, I believe that the application is in compliance with the enablement requirement of Section 112, first paragraph, and I show that the full scope of claims 1-14 is enabled by the specification such that no undue experimentation to prepare and/or practice the invention is required.

6. The application describes how IPAS cells are obtained from exocrine glandular tissue. Using the isolation methods described in the application, I and/or researchers under my direct supervision produced a variety of different IPAS cells from species additional to rats and humans, and from exocrine glandular tissue additional to pancreatic tissue, from which cells from mice, rats, men and from pancreas, salivary glands or skin formations were well characterized. For these

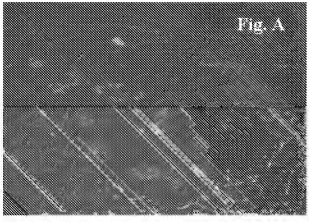
preparations the protocols, which are described in the application, were not needed to be changed in any manner.

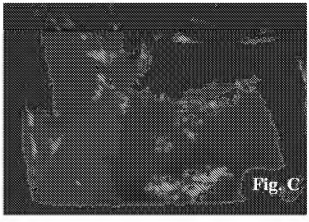
The data in Table 1 below show cells isolated from different tissues with similar morphological and behavior characteristics isolated by the described method, indicating that the invention is enabled for more than just IPAS cells from rat and human pancreatic tissue.

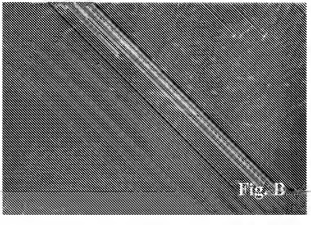
Table 1. Different isolated stem cell lines from exocrine glands.

Species	Organ	Number of Cell lines
Goat	Pancreas	1
	G. Submandibularis	1
	G. Parotis	1
Mouse	Pancreas	14
	G. Submandibularis	1
Human	Pancreas	6
	G. Submandibularis	2
	G. Parotis	3
	Glandulae Buccales	1
Rat	Pancreas	12
Roe Deer	Pancreas	4
Watussi Cattle	Pancreas	1
Platalea Leucorodica (A Heron)	Pancreas	1
Domestic Pig	Pancreas	1
Wild Pig	Pancreas	3
African Green Monkey	Pancreas	1
Guanaco	Pancreas	1
Vietnamese Sica Deer (Cervus Nippon Pseudotaxis)	Pancreas	3
White Naped Crane (Grus Vipio)	Pancreas	1
Chicken	Pancreas	2

7. The invention has enabled IPAS cells to be isolated from human sweat glands (glands without acini) as evidenced by the stem cell marker nestin, which marker has been described by Wiese et al., Cellular and Molecular Life Sciences 2004 Oct; 61(19-20):2510-22. See Figures below, which show nestin-positive staining (red) of human sweat glands (Figs. A and B) and nestin-positive cells (Fig. C), isolated from a human skin and sweat gland preparation.







8. Accordingly, a person reasonably skilled in the art would have been enabled by the original disclosure to isolate IPAS cells from a variety of cell types from a variety of organisms without undue experimentation.

I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine and/or imprisonment under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

26.04.2007
Date

Charli Kruse, Ph.D.

Curriculum Vitae

PD Dr. Charli Kruse

Group Manager of the group "Cell Differentiation & Cell Technology" of the Fraunhofer Institute of Biomedical Engineering, MFC/ICL, Maria-Goeppert-Straße 1, D-23562 Lübeck, Germany

born:	July, 17. 1960 in Wismar/Germany
1982-1987	Study Marine Ecology, University of Rostock
1986-1987	Diploma Thesis at the Institute of Animal Physiology at the University of Rostock
1987-1991	Scientific Assistant at the Institute of Animal Physiology at the University of Rostock
1992	Dr. rer. nat (PhD), University of Rostock
1991-2001	Scientific Assistant (PostDoc) at the Institute of Medical Molecular Biology at the University of Luebeck
2000	Habilitation, University of Luebeck
2000	Venia legendi, University of Luebeck
2001-2005	Associate Professor (C2), University of Luebeck
since 2004	Head of the FhG-IBMT-Group "Cell Differentiation & Cell Technology" at the University of Luebeck
since 2005	Academic Senior Councillor (A14), University of Luebeck

Research Topics: haematology of fishes
physiology of fishes
intracellular transport mechanisms
RNA-protein interaction
cellular biology
stem cell biology

Selected publications in the field of cell manipulation and stem cell biology

1. Kruse, Ch.; Strehlow, B.; Schmidt, H. and Müller, P. K. (1996) Presence of trypsin in distinctive body segments of leptocephalus larvae of Anguilliformes. Aquaculture; 142, 237-244
2. Kügler, S.; Grünweller, A.; Probst, C.; Müller, P. K. and Kruse, C. (1996) Vigilin contains a functional nuclear localisation sequence and is present both in the cytoplasm and the nucleus. FEBS Letters; 382, 330-334
3. Kruse, C., Willkomm, D., Grünweller, A., Vollbrandt, T., Sommer, S., Busch, S., Pfeiffer, T., Brinkmann, J., Hartmann, R.K., and Müller, P. K. (2000) Export and transport of tRNA are coupled to a multi-protein complex. Biochemical Journal; 346, 107-115
4. Kruse, C., Hartmann, R. K. and Müller, P. K. (2001) Nuclear-cytoplasmic translocation of tRNA; Exp. Cell Res., 262, 3-7
5. Kruse, C., Willkomm, D., Gebken, J., Schuh, A., Stoßberg, H., Vollbrandt, T. and Müller, P.K. (2003) The multi-KH-protein vigilin associates with free and membrane

bound ribosomes. Cell. Mol. Life Sci.; 60, 2219-2228
6. Kruse, C., Birth, M., Rohwedel, J., Assmuth, K., Goepel, A., and Wedel, T. (2004) Pluripotency of adult stem cells derived from human and rat pancreas. Appl. Phys. A 2004; 79, 1617-1624
7. Kruse, C., Bodo, E., Petschnik, A. E., Danner, S., Tiede, S. and Paus, R. (2006). „Towards the development of a pragmatic technique for isolating and differentiating nestin-positive cells from human scalp skin into neuronal and glial cell populations: generating neurons from human skin?" Exp. Dermatol.; 15, 794-801
8. Kruse, C., Kajahn, J., Petschnik, A. E., Maaß, A., Klink, E., Rapoport D. H. and Wedel, T. (2006). Adult pancreatic stem/progenitor cells spontaneously differentiate in vitro into multiple cell lineages and form teratoma-like structures. Ann. Anat.; 188, 503-517
9. Guldner, N. W., Kajahn, J., Klinger, M., Sievers, H.-H. and Kruse, C. (2006) Autonomously contracting human cardiomyocytes generated from adult pancreatic stem cells and enhanced in cocultures with myocardial biopsies. Int. J. Artif. Org.; 29: 1158 - 1166
10. Danner, S., Kajahn, J., Geismann, C., Klink, E. and Kruse, C. (2007) Derivation of oocyte-like cells from a clonal pancreatic stem cell line. Mol. Hum. Reprod.; 13: 11-20. Epub 2006 Nov 17
11. Tiede, S., Kloepper, J.E., Bodò, E, Tiwari, S., Kruse, C. and Paus, R. (2007) Hair follicle stem cells: Walking the maze, Eur. J. Cell Biol. (in press)